

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
26 May 2005 (26.05.2005)

PCT

(10) International Publication Number  
**WO 2005/047503 A1**

- (51) International Patent Classification<sup>7</sup>: C12N 15/10, C07K 7/04
- (21) International Application Number: PCT/EP2003/012783
- (22) International Filing Date: 15 November 2003 (15.11.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (71) Applicants (for all designated States except US): POLYPHOR LTD. [CH/CH]; Gewerbstrasse 14, CH-4123 Allschwil (CH). UNIVERSITÄT ZÜRICH [CH/CH]; Rämistrasse 71, CH-8006 Zürich (CH).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): VRLJBLOED, Jan, Wim [NL/CH]; Imbisbühlstrasse 133, CH-8049 Zürich (CH). OBRECHT, Daniel [CH/CH]; Im Eichacker 21, CH-4112 Bättwil (CH). LOCURIO, Sergio [IT/CH]; Rigistrasse 3, CH-8700 Küsnacht (CH). GOMBERT, Frank, Otto [DE/DE]; Am Rebhang 20, 79588 Huttingen (DE). LUDIN, Christian [DE/CH]; Traugott Meyerstrasse 8, CH-4147 Aesch (CH). JUNG, Françoise [FR/CH]; Mutschellenstrasse 177, CH-8038 Zürich (CH).
- (74) Agent: BRAUN, André; Braun & Partner, Reusstrasse 22, CH-4054 Basel (CH).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— with international search report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: TEMPLATE FIXED BETA-HAIRPIN LOOP MIMETICS AND THEIR USE IN PHAGE DISPLAY

(57) Abstract: Template-fixed  $\beta$ -hairpin mimetics of the general formula  $R^1$ -Cys-Z-Cys- $R^2$  (I) wherein the two Cys residues are bridged by a disulfide bond thereby forming a cyclic peptide;  $R^1$  and  $R^2$  are preferably Glu-Thr and Thr-Lys; or Lys-Thr and Thr-Glu; or Thr-Glu and Lys-Thr; or Thr-Lys and Glu-Thr; or Leu-Glu and Lys-Val; or Val-Lys and Glu-Leu; or Glu-Leu and Val-Lys; or Lys-Leu and Val-Glu; or Asn-Gly and Lys-Val; or Val-Gly and Lys-Asn; or Gly-Asn and Val-Lys; or Gly-Val and Asn-Lys; or Gly-Gly and Gly-Gly; or Glu-Leu-Lys and Glu-Val-Lys; or Lys-Val-Glu and Lys-Leu-Glu; or Leu-Glu-Lys and Glu-Lys-Val; or Val-Lys-Glu and Lys-Glu-Leu; or Glu-Lys-Leu and Val-Glu-Lys; or Lys-Glu-Val and Leu-Lys-Glu; or Lys-Glu-Leu and Val-Lys-Glu; or Glu-Lys-Val and Leu-Glu-Lys; or Lys-Val-Gly and Gly-Leu-Glu; or Glu-Leu-Gly and Gly-Val-Lys; or Val-Lys-Gly and Gly-Glu-Leu; or Leu-Glu-Gly and Gly-Lys-Val; or Val-Gly-Lys and Glu-Gly-Leu; or Leu-Gly-Glu and Lys-Gly-Val; or Gly-Gly-Gly and Gly-Gly-Gly; and Z is a chain of n amino acid residues with n being an integer from 4 to 20 and with each of these n amino acid residues being, independently, derived from any naturally occurring L-  $\alpha$ -amino acid are provided. Libraries comprising a plurality of these templates can be used for the construction of phage display derived template-fixed  $\beta$ -hairpin mimetics generating phage display libraries with very high binding constants to targets, thus combining the advantage of screening of large phage display derived template-fixed  $\beta$ -hairpin libraries which in turn considerably facilitates structure-activity studies, and hence the discovery of new molecules with potent activities and with novel selectivities towards different types of targets.

WO 2005/047503 A1